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VALVULAR HEART DISEASE

PLASMA BIOMARKERS OF COLLAGEN AND FIBRONECTIN BIOSYNTHESIS ARE UNRELATED TO TISSUE IMUNOHISTOCHEMICAL PROTEIN QUANTIFICATION OR MRNA DETERMINED BY MYOCARDIAL BIOSPY MICROARRAY IN AORTIC VALVE DISEASE

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Authors: *Daniel Catanzaro, Christopher Stuart, Ji-Sun Hong, Ada Ene, John Carter, Edmund Herrold, Phyllis Supino, Jason Lazar, Lou Salciccioli, Wilson Ko, Arash Salemi, Leonard Girardi, Karl Krieger, O. Wayne Isom, Jeffrey Borer, SUNY Downstate, Brooklyn, NY, Weill Cornell Medical College, New York, NY*

Background: Abnormal collagen (COL) and fibronectin expression may occur in the progression of aortic regurgitation (AR) and aortic stenosis (AS). Plasma levels of procollagen type I amino terminal propeptides (PINP) and COL I carboxy-terminal telopepetide (ICTP), are thought to provide indices of COL I synthesis and degradation, respectively. However, the relation of plasma concentrations of these biomarkers to myocardial expression of their respective genes is not known.

Method: Tru-cut biopsies were obtained from the LV free wall from pts with normal LV performance undergoing aortic valve replacement (AVR) for isolated, pure AS (n=9) or isolated, pure AR (n=10), and from "control" pts with coronary artery disease (CAD) but no infarction undergoing bypass grafting (CABG) (n=7). RNA was prepared and used to synthesize labeled cRNA to probe Affymetrix microarrays (Human Genome U133 Plus 2.0). Tissues were stained for fibrillar COL by picrosirius red, and for COL I, COL III and fibronectin by immunohistochemistry. Plasma prepared from aretrial blood immediately before the induction of cardioplegia was used to measure PINP, ICTP and fibronectin using commercially available ELISA kits.

Results: Plasma concentrations of PINP were 1.5-fold higher in pts with AR (p=0.05) or AS (p=0.07) compared to CAD controls. ICTP and FN concentrations were statistically indistinguishable between diagnoses. Plasma concentrations of PINP, ICTP or FN were unrelated to histological or immunocytochemical staining for myocardial COL I or fibronectin; no association was apparent with COL I or fibronectin mRNA, or mRNAs encoding any proteins potentially involved in the synthesis or degradation of COL or fibronectin.

Conclusion: Although PINP concentrations are abnormal in plasma samples from pts undergoing AVR for AR or AS compared to pts undergoing CABG, the poor correlation with myocardial tissue protein and mRNA concentrations suggest that plasma concentrations may not be due to secretion from myocardial tissue or that the relation of secretion to tissue metabolism may be particularly complex. More extensive sampling will be needed to resolve these issues.